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Susan M. Barry
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IN THE UNITED STATES PATENT AND TRADEMARK OFFICE

Applicant:	Freda Miller et al.	Art Unit:	1646
Serial No.:	08/920,272	Examiner:	J. Murphy
Filed:	August 22, 1997		
Title:	PHARMACEUTICALS CONTAINING MULTIPOTENTIAL PRECURSOR CELLS FROM TISSUES CONTAINING SENSORY RECEPTORS		

Assistant Commissioner of Patents and Trademarks
Washington, DC 20231

DECLARATION OF FREDA MILLER UNDER 37 CFR §1.132

The undersigned, Freda D. Miller, Ph.D., hereby declares and states that:

1. I am an Associate Professor in the Department of Neurology and Neurosurgery at McGill University, Coordinator of the Center for Neuronal Survival at the Montreal Neurological Institute, and an inventor on the above-captioned patent application. I have worked at the Montreal Neurological Institute since 1993.

2. I have read and understood the Office Action dated December 6, 1999.

3. At the time of filing, the level of skill of one in the field of neural transplantation was high. This is supported by the prior art, which taught the transplantation of neural cells into the brain of a mammal (for review, see Lindvall, Cell Transplant. 4:393-400, 1995, a copy of which is enclosed). In one art example, dopaminergic neurons were transplanted into the brains of rodents in which dopaminergic neurons were previously selectively ablated (see, for example, Zhou, Neurosci. Lett. 163:81-84, 1993; Nikkah et al., J. Neurosci. 14:3449-3461, 1994; Constantini et al., Exp. Neurol. 127:219-223, 1995; and Nikkah et al., J. Neurosci. 15:3548-3561, 1995, copies of which are enclosed). The transplanted neurons were observed to sprout neurites and form synaptic connenctions. Transplantation resulted in a reversal of behavioral deficits caused by the previous loss of dopaminergic neurons. In a second example, fetal cells have been transplanted into the brains of (i) patients suffering from Parkinson's disease (Kordower et al., J. Comp. Neurol. 370:203-230, 1996, a copy of which is enclosed) and (ii) individuals who lost dopaminergic neurons following self-administration of a "designer" drug containing high levels of MPTP (Lindvall, *supra*). Recipients exhibited functional improvement following transplantation.

4. At the time of filing, it was recognized that two obstacles to neural cell therapy were the lack of a sufficient number of cells for transplantation and, following transplantation, the rejection of the non-autologous donor cells by the host (see, for example, Lindvall, *supra*; Duan et al., Exp. Brain Res. 104:227-242, 1995). As part of the present invention, I have developed a method for culturing the neural stem cells from peripheral tissue containing sensory receptors. I have cultured mouse neural stem cells from peripheral tissue for approximately eight months. Surprisingly, after extensive culturing, these cells maintain their ability to produce a wide range of cell types not observed in the tissue from which the cells were derived. During this time in culture, the number of neural stem cells increased approximately 10^{16}-fold, resulting in ample cells for transplantation. Regarding host rejection, Duan (*supra*) demonstrated that the loss of cells following transplantation is due in large part to a host response to the donor tissue. The autologous cell transplantation enabled by the present invention would not be expected to induce such a host response. Thus, the present invention overcomes two problems associated with neural cell therapy: obtaining a quantity of cells capable of yielding neural cells, and obtaining such cells from the patient, thus avoiding host rejection.

5. I hereby declare that all statements made herein of my own knowledge are true and that all statements made on information and belief are believed to be true; and further

that these statements were made with the knowledge that willful false statements and the like so made are punishable by fine or imprisonment, or both, under Section 1001 of Title 18 of the United States Code and that willful false statements may jeopardize the validity of the application of any patents issued thereon.

Freda Miller

FREDA D. MILLER

DATE: JUNE 6 2000